Dr. Olavi Makela Institutum Sero-Bacteriologicum Universitatis Helsinki, Finland

Dear Dr. Makela:

Thank you for your letter of August 3rd. Your suggestions are very well taken and entirely acceptable. In fact it is not so much a matter that they have not been taken into account as a question of judgment in what detail the theory should be developed as a particular version-Dr. Burnet, I think, has put even more stress on continued mutation of the clones, and the progressive perfection of the corresponding population of antibodies.

The experiment you indicated might be called a test for an immunological conditioned reflex. I do not know of any very incisive attempts in this direction. Talmage had told me that he was thinking of going somewhat more deeply into this particular question. It is, of course, in some degree related to the question of heteroligating antibodies which have been so controversial. Some of the experimental data already published which relate indirectly to this problem are a bit confusing. For example, there is the paper by Dixon and Maurer in the Journal of Immunology, June 1955. However, I find it difficult to draw a clear conclusion from those experiments.

A related question which is equally uncertain is whether the response to a given antigen A includes any antibodies which have a higher affinity for a cross-reacting antigen B than they do for A. This is predicted by the selection hypothesis; It is not incompatible with instructive hypotheses but it still seems to be a subject of empirical argument.

We are looking forward to your arrival. Dr. Nossal will be here about August 19th. However, I have to say that there has been a small delay in the final completion of some of our facilities and it would not be tragic if you took your leisure about arriving. However, we will be ready for you and in any case, you will doubtless want some few days to settle in before you can energetically begin your laboratory work.

Yours sincerely,

Joshua Lederberg Professor of Genetics

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